



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,035	05/02/2005	Fei Huang	D0185 PCT	8131
23914 7590 07/10/2008				
LOUIS J. WILLE				
BRISTOL-MYERS SQUIBB COMPANY				
PATENT DEPARTMENT				
P O BOX 4000				
PRINCETON, NJ 08543-4000				
EXAMINER				
LIU, SUE XU				
ART UNIT		PAPER NUMBER		
1639				
NOTIFICATION DATE		DELIVERY MODE		
07/10/2008		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@BMS.COM
patents@bms.com
eileen.immordino@bms.com

Office Action Summary

Application No.

10/501,035

Applicant(s)

HUANG ET AL.

Examiner

SUE LIU

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-893)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim Status

1. Claims 1-42 have been cancelled as filed on 3/14/08.
Claims 43 and 44 have been added as filed on 3/14/08.
Claims 43 and 44 are currently pending.
Claims 43 and 44 are being examined in this application.

Election/Restrictions

2. Applicants have canceled all claims and added new claims 43 and 44, which are examined in this application.

Priority

3. This application is filed under 35 U.S.C 371 of PCT/US031/01981 (filed on 01/17/2003), which claims priority to US provisional applications 60/350,061 (filed on 1/18/2002).
4. Applicant's submission of sequence alignment to indicate support for the instant claimed SEQ ID NOs: 204 and 3 in the provisional application is acknowledged.

Specification

5. The substitute specification filed 3/14/08 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: a clean copy of the substitute specification has not been supplied (in addition to the marked-up copy). See also MPEP 608.01q.

Claim Objection(s) / Rejection(s) Withdrawn

6. In light of applicants' cancellation of all previous pending claims, all previous claim objections or rejections are moot.

However, new claim objection(s) or rejection(s) are necessitated by applicants' amendments to the claims (i.e. the newly added claims 43 and 44) as set forth below.

New Claim Objection(s) / Rejection(s)

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

8. Claims 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is necessitated by applicant's amendments to the claims.

Claims 43 and 44 have been newly added and recite "while decreased expression of said gene expression product in said sample relative to a standard is indicative of resistance to a protein tyrosine kinase inhibitor". However, the instant specification does not appear to provide support for the claimed "decreased expression of said gene expression... is indicative of resistance". The citations pointed out by applicants (Reply, filed on 9/6/07) for support of the newly added claims do not appear to offer support for the said specific citation. For example Applicants pointed to the Tables (e.g. 3-6 and 10-12) of the instant specification, which Tables only indicate that the listed genes are "highly expressed" (i.e. increased expression) in resistant cells (see Table 12, for example; also see pp.13+). In addition, the instant specification states "OF the 123 polynucleotides and polypeptides, 60 were highly expressed in the cell lines that were classified as sensitive to BMS-A or BMS-D, and 63 polynucleotides and polypeptides were highly expressed in the cell lines that were classified as resistant to BMS-A or BMS-D." (spec., p.22. lines 3+). It is not clear which specific passage of the instant specification discloses that "decreased expression" indicates resistance.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claims 43 and 44 represent new matter.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in *italic*):

Applicants assert the instant specification provides support for the instant claimed "while decreased expression of said gene expression product in said sample... is indicative of resistance" (Reply, pp.9+).

Applicants pointed to the recitation on page 20 of the instant specification: "An 'idealized expression pattern' corresponds to a gene that is uniformly high in one class (e.g. sensitive) and uniformly low in the other class (e.g., resistant)." For support of the instant claimed "decreased expression". However, the instant specification does not provide support for this "idealized expression pattern" for any of the listed genes including the instant claimed "BMP-2" gene (SEQ ID NO:204) and polypeptide with SEQ ID NO:247. Furthermore, the above recitation of "an idealized expressed pattern" indicates that said "low" expression in "other class" (e.g., resistant) is only a postulation or wish plan for finding such a gene. As discussed above, all of the gene markers listed in the Tables of the instant specification are highly expressed in either Sensitive or Resistant cells (see Spec., p.22). For example, the instant specification recites that the BMP-2 gene is highly expressed in cells that are sensitive to certain compounds (e.g. Table 3), but nowhere in the instant specification is disclosed that the expression of BMP-2 gene is decreased in cells that resistant to various kinase inhibitors.

Applicants also pointed to the instant disclosure on page 28 to assert that because a number polynucleotides are known substrates to src tyrosine kinase family, "one of skilled in the

Art Unit: 1635

art would credibly believe that applicants were in possession of a method... based upon the decreased expression of a sensitive informative gene” (Reply, p.10). However, the scientific basis for this assertion is not clear. It is not clear how one of skilled in the art would leap from a protein/gene being a “substrate” for src tyrosine kinase family to its decreased gene expression being an indicator for the resistance to src tyrosine kinase inhibitor. In addition, the relationship among src kinase family proteins and their substrates are not completely understood. The Brown reference cited in the instant specification also does not particularly list the BMP-2 gene as a substrate for the src tyrosine kinase family. Thus, the instant disclosure does not provide support for the newly added limitation either explicitly or inherently.

Second paragraph of 35 U.S.C. 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 43 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by applicant’s amendments to the claims.

The claim language of Claims 43 and 44 are unclear and indefinite. For example, Claims 43 and 44 recite “while decreased expression of said gene expression product in said sample relative to a standard is indicative of resistance to a protein tyrosine kinase inhibitor”, which recitation seems to contradict the definition and disclosure of the instant specification. The instant specification, for example, lists “polynucleotides” that are used to indicate “sensitivity/resistance” of cells to kinase inhibitors in various Tables. The instant specification

discloses the “polynucleotides” are all “highly expressed” (i.e. increased expression) in resistant cells (see Table 12, for example; see p. 22, II 3+), which are in direct contradiction with the recitation “decreased expression... indicative of resistance” of the instant claim. Thus, one of ordinary skill in the art would not be able to apprise the metes and bounds of the claimed invention. See MPEP 2173.03.

Discussion and Answer to Argument

12. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants assert the instant claim language is clear and is not in contradiction with the instant specification. (Reply, pp.12+).

Applicants traversed this rejection mostly citing the disclosure in the instant specification that is relevant to correlating high gene expression with cells that are sensitive to kinase inhibitors. However, the instant claims recite “decrease expression of said gene expression product... indicative of resistance to a protein tyrosine kinase inhibitor”. However, the instant specification defines the all the listed polynucleotides (in various Tables) are highly expressed in either sensitive or resistant cell lines. Thus, it is not clear if “highly expressed” (i.e. increased expression) is in resistant cells or if “decreased expression” is in resistant cells.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Shyjan, Imai, Roth and Mahon

14. Claims 43 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Shyjan et al (US 20020006613; 1/17/2002; 1/17/2002; filed 8/13/2002; or earlier priority date), in view of Imai et al (Pathology International. Vol.51: 643-648; 8/2001), Roth et al (US 20020051978; 5/2/02; filed on 2/16/01; or earlier priority date) and Mahon et al (Blood. Vol. 96(3): 1070-1079; 2000). This rejection is necessitated by applicant's amendments to the claims.

The instant claims recite "A method of identifying colon cancer cells that are either resistant or sensitive to a protein tyrosine kinase inhibitor comprising the step of

(a) determining the expression profile of an expression product from at least one informative polynucleotide in a colon cancer sample, wherein said at least one informative polynucleotide is the polynucleotide encoding bone morphogenetic protein 2 (SEQ ID NO:204);

(b) comparing the expression level of said expression product to a standard; and

(c) determining whether said colon cancer cells are resistant or sensitive to a protein tyrosine kinase inhibitor, *wherein increased expression of said expression product in said sample relative to said standard is indicative of sensitivity to a protein tyrosine kinase inhibitor, while decreased expression of said gene expression product in said sample relative to said standard is indicative of resistance to a protein tyrosine kinase inhibitor.*

The recitation “identifying colon cancer cells that are either resistant or sensitive to a protein tyrosine kinase inhibitor” in the preamble of **clm 43** is construed as intended uses of the instant claimed method for the purpose of the following prior art rejections, because the said recitations do not appear to impart structural limitations to the claimed method steps. As discussed below in the body of the rejection, the teachings of the combination of references indicate that the methods of the prior art are capable of performing the instant claimed intended uses.

See MPEP 2111.02 II: “If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention’s limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999).”

In this case, the body of the claims set forth all the method structural limitation of the claimed method. The body of the claim (e.g. Claim 43) recites “determining the expression profile of an expression product from at least one informative polynucleotide in a colon cancer

sample...” That is the body of the claim recites all the required method steps/reagents including “determining the expression profile”, “SEQ ID NO:204”, “a colon cancer sample”, etc.. The recitation of “identifying colon cancer cells that are either resistant or sensitive to a protein tyrosine kinase inhibitor” does not offer additional structural limitation to the claimed method, and only seems to provide the “intended result” (or use) of the process step in the body of the instant claims. That is the “determining expression profile” step of the specific recited polynucleotides (e.g. polynucleotide encoding SEQ ID NO:204) in a colon cancer cell would result in the identification of the “colon cancer” as either “resistant or sensitive to a protein tyrosine kinase inhibitor”. This claim interpretation is supported by the instant specification where a cell’s resistance/sensitivity to a kinase inhibitor is correlated to various gene expression profiles (e.g. p.19, lines 11+; Tables).

In addition, the underlined region of the recitation “wherein increased expression of said expression product in said sample relative to a standard is indicative of sensitivity to a protein tyrosine kinase inhibitor, while decreased expression of said gene expression product in said sample relative to a standard is indicative of resistance to a protein tyrosine kinase inhibitor” in the instant claims 43 and 44 also do not appear to provide additional structural limitations such as additional method steps/reagents.

See MPEP 2106 II: “Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation.” (emphasis in original);

See also MPEP 2111.04: “Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not

limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:

- (A) "adapted to" or "adapted for" clauses;
- (B) "wherein" clauses; and
- (C) "whereby" clauses."

"... However, the court noted (quoting *Minton v. Nat 'l Ass 'n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a 'whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" (emphasis added).

In this case, the phrase "relative to a standard" (i.e. comparing the sample cell gene expression to a standard) can be construed as another "process step" that is "positively recited". The recitations such as "indicative of sensitivity to a protein tyrosine kinase inhibitor" "simply expresses the intended result of the a process step positively recited".

Therefore, the instant claim 43 can be construed to recite a method comprising the following method steps/reagents:

- A.) determining the expression profile of at least one polynucleotide comprising a polynucleotide encoding for a protein of SEQ ID NO: 204 (or bone morphogenetic protein 2);
- B.) comparing the expression profile of A) to "a standard";
- C.) determining whether said colon cells are resistant or sensitive to a protein tyrosine kinase inhibitor.

The following art rejection is discussed in light of the above claim interpretation.

Shyjan et al, throughout the publication, teach using gene expression profile of markers (or nucleic acids) to determine if cancer cells are sensitive or resistant to a therapeutic agent. (e.g. Abstract). The reference teaches determining gene expression levels from cancer cell samples (e.g. p.1, [0008]+; claims 1+; p.3, [0030]+) by measuring gene expression products such as mRNA levels (e.g. pp.5-6, [0048]+), which read on the steps of determining gene expression profile of an expression product of an informative polynucleotide as recited in **clm 43**. The reference also teaches comparing the expression profile of the genes of colon cancer cell lines to standards (e.g. pp.19-20; [0212]).

As discussed above, the recitation “wherein increased expression ... is indicative of sensitivity to a protein tyrosine kinase inhibitor, while decreased expression ...” is construed as intended use or result of the instant claimed method. See MPEP 2111.04: “However, the court noted (quoting *Minton v. Nat ’l Ass ’n of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a ‘whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.’” (emphasis added).

Shyjan et al do not explicitly teach step (c) of **clm 43** of determining whether said colon cancer cells are resistant or sensitive to a protein tyrosine kinase inhibitor. The reference also does not explicitly teach monitoring the gene expression of BMP-2 (i.e. SEQ ID NO:204) as recited in **clm 43**, and another additional polynucleotide with sequences recited in the specific SEQ ID Nos as recited in **clm 44**.

However, **Imai et al**, throughout the publication, teach monitoring gene expression profile of various genes in colon cancer sample. Imai et al, throughout the publication, teach monitoring gene expression profile of various genes in colon cancer samples (e.g. Abstract). The reference teaches determining the gene expression of various bone morphogenetic proteins (BMPs) in colon tumors and/surrounding cells from colon tissues by using immunohistochemical staining of the proteins (i.e. expression products) (e.g. Figure 1; pp.644-645), which read on the steps of determining gene expression profile of an expression product of an informative polynucleotide as recited in **clm 43**.

The reference also teaches comparing the gene expression of BMP-2 gene in various cells such as tumor cells and “mesenchymal fibroblast cells” (e.g. Figure 4; p.645, para 2), which read on the comparing with “a standard” of **clm 43** because the mesenchymal fibroblast cells can be considered as a standard as the term “a standard” is broadly used in the instant disclosure. The reference also inherently teaches BMP-2 has the amino acid sequence listed in SEQ ID NO:204, as evidenced by the instant disclosure reciting BMP-2 protein has the sequence listed in SEQ ID NO:204 (See p.104, Table 3 of the spec.). The reference teaches that the Bone Morphogenetic Proteins expressed are human proteins (e.g. Abstract), and the instant specification also teaches that the BMP-2 protein is of human origin as reflected by its GenBank accession number “M22489” (see p.104, Table 3) and citation in the instant Sequence Listing. Thus, the BMP-2 protein of the reference inherently comprise the sequence recited in SEQ ID NO:204 without evidence to the contrary.

The Imai reference also teaches that BMP-2 gene is differentially expressed in colon tumor tissues.

Roth et al, throughout the publication, teach identifying cells that are sensitive to cancer therapeutic agents using gene expression profile. (e.g. Abstract). The reference teaches measuring gene expression in various cancer cells including colon/colorectal tumor cells (e.g. p.5, [0061]). The reference also teaches the gene markers used for assessing gene expression profile to determine drug sensitivity includes the polynucleotide of GenBank accession number “D13413” (e.g. Tables 6 and 8), which the GenBank accession number D13413 corresponds to the polynucleotide encoding the protein of the instant SEQ ID No:247 of **clm 44**, as evidenced by Table 3 of the instant specification. The reference also teaches that the gene with accession number D13413 is differentially expressed in cells that have differential response to cancer therapeutic drugs. (e.g. Table 6; p.29).

Mahon et al, throughout the publication, teach characterizations of cancer cell lines with differential sensitivity to a tyrosine kinase inhibitor (e.g. Abstract). The reference teaches studying the effects of a tyrosine kinase inhibitor on different cell lines, which exhibit various degrees of sensitivity or resistance to the inhibitor (e.g. pp.1072+; Figure 3). The Mahon reference also teaches the need to study cells’ resistance and sensitivity to tyrosine kinase inhibitors because the inhibitor’s potential as cancer treating drugs and understanding of drug resistance is important (e.g. p.1070).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to determining gene expression profiles of various genes of interest and to determine whether colon cancer cells are sensitive or resistant to various kinase inhibitors.

A person of ordinary skill in the art would have been motivated at the time of the invention to monitor gene expression profile of BMP-2 gene in colon/colorectal cancer cells, because BMP-2 gene provides the advantage as a useful and unique marker that is differentially expressed in the colon tissues.

A person of ordinary skill in the art would have been motivated at the time of the invention to monitor gene expression profile of a polynucleotide with GenBank accession number D13413 (or the polynucleotide encoding for SEQ ID NO:247) in colon/colorectal cancer cells, because the marker, D13413 provides the advantages of having differential gene expression profile in cells with different reactivity (sensitivity or resistance) to cancer therapeutic agents, as taught by Roth et al. In addition, one of ordinary skill in the art would have been motivated at the time of the invention to use D13413 polynucleotide in addition to BMP-2 gene for achieving the predictable result of measuring differential gene expression profile in colon/colorectal cancer cells.

A person of ordinary skill in the art would have been motivated at the time of the invention to determine colon cancer cells' sensitivity or resistance to tyrosine kinase inhibitors, because Mahon et al teach the need to determining resistance/sensitivity of cells to tyrosine kinase inhibitors as they are potential cancer therapeutic agents. Additionally, Shyjan et al, also teach the need to identify markers (genes) that can be used to determining whether cancer cells (especially colon cancer cells) are sensitive or resistant to a therapeutic agent. Further, because both Shyjan and Mahon references teaches method of determining cancer cell sensitivity/resistance to various compounds/drugs/inhibitors, it would have been obvious to one skilled in the art to substitute one method (of one type of cancer cells testing with one type of

drug such as a kinase inhibitor) for the other (of colon cancer cells testing with a kinase inhibitor) to achieve the predictable result of determining colon cancer cell sensitivity/resistance to tyrosine kinase inhibitors.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since Shyjan et al, Imai et al and Roth et al. all have demonstrated the success of measuring gene expression profiles (e.g. measuring gene expression products) in colon cancer cells; Shyjan et al., have demonstrated the success of determining sensitivity/resistance of colon cancer cells to various compounds/drugs, and Mahon et al, have demonstrated determining sensitivity/resistance of cancer cells to tyrosine kinase inhibitors.

Discussion and Answer to Argument

15. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in *italic*):

Applicants traversed the previous set forth claim rejection under 35 USC 103(a) based on newly added claim limitations. (Reply, pp.21+).

Applicants are respectfully directed to the above rejection for detailed discussion of how the combination of the cited references render the instant claimed invention obvious.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

Art Unit: 1635

improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 43 and 44 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41, 43 and 44 of copending Application No10/348,119 (US 20070166704). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed method of the ‘119 co-pending application read on the instant claimed invention. This rejection is necessitated by applicant’s amendments to the claims.

Claim 41 of the ‘119 application recites: “A method of identifying colon cancer cells that are either resistant or sensitive to a protein tyrosine kinase inhibitor comprising the step of determining the expression profile of an expression product from an informative polynucleotide predictor set in a colon cancer sample, wherein said informative polynucleotide predictor set consists of: SEQ ID NO:1... SEQ ID NO:3...”, which read on the claim limitation of the instant **clms 43 and 44** because SEQ ID Nos. 1 and 3 encode for the same proteins of SEQ ID Nos:202

and 204 of the instant claims. (See Table 3 of the '119 application and Table 3 of the instant spec. for SEQ ID No correspondence between the specific polynucleotides and polypeptides).

Similarly, claims 41 and 42 recite method using the specific SEQ ID Nos, which read on the instant claimed method of **clms 43 and 44**.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Discussion and Answer to Argument

18. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue because the above rejection is a "provisional" ODP rejection, "no action is currently required on behalf of Applicants." (Reply, p.24.)

It is noted applicants have not traversed the merits of the above ODP rejection. As stated in the MPEP 804: "The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications." Thus, the above ODP rejection is set forth for the reasons above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sue Liu
Patent Examiner, AU 1639
6/23/08

/JD Schultz, PhD/

Supervisory Patent Examiner, Art Unit 1635